Clinical trial results:
Effect of semaglutide on functional capacity in patients with type 2 diabetes and peripheral artery disease

Summary

EudraCT number	2019-003399-38
Trial protocol	DE AT HU NO BE DK LV
Global end of trial date	12 July 2024

Results information

Result version number	v1 (current)
This version publication date	24 July 2025
First version publication date	24 July 2025

Trial information

Trial identification

Sponsor protocol code	NN9535-4533

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04560998
WHO universal trial number (UTN)	U1111-1238-7071
Other trial identifiers	Japanese trial registration number: jRCT2031200141

Notes:

Sponsors

Sponsor organisation name	Novo Nordisk A/S
Sponsor organisation address	Novo Alle, Bagsvaerd, Denmark, 2880
Public contact	Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.com
Scientific contact	Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 September 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 July 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to demonstrate the effect of subcutaneous (s.c., under the skin) semaglutide 1 mg once-weekly on walking ability compared with placebo, both added to standard-of-care, in patients with type 2 diabetes (T2D) and peripheral arterial disease (PAD) with intermittent claudication.

Protection of trial subjects:

The study was conducted in accordance with the Declaration of Helsinki and International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Good Clinical Practice, including archiving of essential documents.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	01 October 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 5
Country: Number of subjects enrolled	Belgium: 30
Country: Number of subjects enrolled	Canada: 61
Country: Number of subjects enrolled	China: 18
Country: Number of subjects enrolled	Czechia: 27
Country: Number of subjects enrolled	Germany: 23
Country: Number of subjects enrolled	Denmark: 44
Country: Number of subjects enrolled	Spain: 38
Country: Number of subjects enrolled	Greece: 66
Country: Number of subjects enrolled	Hungary: 61
Country: Number of subjects enrolled	India: 33
Country: Number of subjects enrolled	Japan: 79
Country: Number of subjects enrolled	Latvia: 35
Country: Number of subjects enrolled	Malaysia: 33
Country: Number of subjects enrolled	Norway: 11
Country: Number of subjects enrolled	Poland: 100
Country: Number of subjects enrolled	Sweden: 8

Country: Number of subjects enrolled	Thailand: 30
Country: Number of subjects enrolled	Taiwan: 38
Country: Number of subjects enrolled	United States: 52
Worldwide total number of subjects	792
EEA total number of subjects	448

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	285
From 65 to 84 years	499
85 years and over	8

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 129 sites in 21 countries.

Pre-assignment

Screening details:

Participants were randomized in a 1:1 ratio to receive treatment with either semaglutide or placebo as an adjunct to standard-of-care.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Semaglutide

Arm description:

Participants received once-weekly (OW) subcutaneous injection (s. c.) of semaglutide for 52 weeks. Participants received a dose of 0.25 milligrams (mg) from week 0 to week 4, then the dose was increased to 0.5 mg from week 4 to week 8. From week 8 to week 52, the dosage was 1.0 mg.

Arm type	Experimental
Investigational medicinal product name	Semaglutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Once-weekly subcutaneous injection of semaglutide was administered for 52 weeks

Arm title	Placebo

Arm description:

Participants received once-weekly (OW) subcutaneous injection (s. c.) of placebo matched for semaglutide for 52 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Once-weekly subcutaneous injection of placebo matched for semaglutide was administered for 52 weeks.

Number of subjects in period 1	Semaglutide	Placebo
Started	396	396
Full analysis set	396	396
Safety analysis set	396	395
Completed	366	379
Not completed	30	17
Physician decision	4	-
Consent withdrawn by subject	18	12
Lost to follow-up	8	5

Baseline characteristics

Reporting groups	
Reporting group title	Semaglutide
Reporting group description:	
Participants received once-weekly (OW) subcutaneous injection (s. c.) of semaglutide for 52 weeks. Participants received a dose of 0.25 milligrams (mg) from week 0 to week 4, then the dose was increased to 0.5 mg from week 4 to week 8. From week 8 to week 52, the dosage was 1.0 mg.	
Reporting group title	Placebo
Reporting group description:	
Participants received once-weekly (OW) subcutaneous injection (s. c.) of placebo matched for semaglutide for 52 weeks.	

Reporting group values	Semaglutide	Placebo	Total
Number of subjects	396	396	792
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	152	133	285
From 65 years	244	263	507
Age Continuous			
Units: Years			
arithmetic mean	66.2	67.0	
standard deviation	± 9.71	± 8.96	-
Sex: Female, Male			
Units: Participants			
Female	107	88	195
Male	289	308	597

End points

End points reporting groups

Reporting group title	Semaglutide
Reporting group description:	
Participants received once-weekly (OW) subcutaneous injection (s. c.) of semaglutide for 52 weeks. Participants received a dose of 0.25 milligrams (mg) from week 0 to week 4, then the dose was increased to 0.5 mg from week 4 to week 8. From week 8 to week 52, the dosage was 1.0 mg.	
Reporting group title	Placebo
Reporting group description:	
Participants received once-weekly (OW) subcutaneous injection (s. c.) of placebo matched for semaglutide for 52 weeks.	

Primary: Change in maximum walking distance on a constant load treadmill test

End point title	Change in maximum walking distance on a constant load treadmill test
End point description:	
Constant-load treadmill test with fixed speed (3.2 km/h, 2 mph), fixed inclination (12%) is a standardised method for functional assessment of patients with peripheral artery disease. Participants continue on treadmill after indicating onset of pain and should continue as long as possible until pain limits further activity. This distance is the maximum walking distance. Endpoint was evaluated based on data from in-study observation period. In-study observation period is defined as period from date of randomisation to one of the following dates, whichever comes first: date of follow-up visit, date when participant withdrew consent, date of last contact with participant for participants who were lost to follow-up (participant did not complete the trial and did not withdraw consent), date of death. Full Analysis Set (FAS). Overall Number of Participants Analyzed = number of participants with available data for this endpoint.	
End point type	Primary
End point timeframe:	
From baseline (week 0) to end of treatment (week 52)	

End point values	Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	338	345		
Units: Ratio of maximum walking distance				
median (inter-quartile range (Q1-Q3))	1.21 (0.95 to 1.55)	1.08 (0.86 to 1.36)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Semaglutide v Placebo

Number of subjects included in analysis	683
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	The Hodges-Lehmann estimate
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.056
upper limit	1.211

Secondary: Follow-up change in maximum walking distance on a constant load treadmill test

End point title	Follow-up change in maximum walking distance on a constant load treadmill test

End point description:

Constant-load treadmill test with fixed speed (3.2 km/h, 2 mph), fixed inclination (12%) is a standardised method for functional assessment of patients with peripheral artery disease. Participants continue on the treadmill after indicating onset of pain and should continue as long as possible until pain limits further activity. This distance is maximum walking distance. Endpoint measure was evaluated based on data from in-study observation period. In-study observation period is defined as the period from date of randomisation to one of following dates, which-ever comes first: date of follow-up visit, date when participant withdrew consent, date of last contact with participant for participants who were lost to follow-up (participant did not complete the trial and did not withdraw consent), date of death. Full Analysis Set (FAS). Overall Number of Participants Analyzed = number of participants with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of follow-up (week 57)

End point values	Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	329	333		
Units: Ratio of maximum walking distance				
median (inter-quartile range (Q1-Q3))	1.16 (0.92 to 1.48)	1.10 (0.87 to 1.40)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Semaglutide v Placebo

Number of subjects included in analysis	662
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.038
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	The Hodges-Lehmann estimate
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.004
upper limit	1.156

Secondary: Change in Vascular Quality of Life Questionnaire-6 (VascuQoL-6) score

End point title	Change in Vascular Quality of Life Questionnaire-6 (VascuQoL-6) score

End point description:

VascuQoL-6 is a peripheral artery disease-specific questionnaire with 6 items covering social, emotional, functional, pain/symptom-related aspects of the patient´s overall quality of life. Each item has a 4-point response scale (where 1 = worst score and 4 = best score). Endpoint analysed is the total score (range: 6-24) generated by summing the scores from all items. Higher score indicates better health status. Endpoint was evaluated based on data from in-study observation period. In-study observation period is defined as the period from date of randomisation to one of following dates, whichever comes first: date of follow-up visit, date when participant withdrew consent, date of last contact with participant for participants who were lost to follow-up (participant did not complete trial and did not withdraw consent), date of death. Full Analysis Set (FAS). Overall Number of Participants Analyzed = number of participants with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 52)

End point values	Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	362	362		
Units: Scores on a scale				
median (inter-quartile range (Q1-Q3))	2.0 (0.00 to 4.00)	1.0 (-1.00 to 4.00)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Semaglutide v Placebo

Number of subjects included in analysis	724
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0108
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	The Hodges-Lehmann estimate
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.478
upper limit	1.518

Secondary: Follow-up change in pain-free walking distance on a constant load treadmill test

End point title	Follow-up change in pain-free walking distance on a constant load treadmill test

End point description:

The constant-load treadmill test with fixed speed (3.2 km/h, 2 mph), fixed inclination (12%) is a standardised method for functional assessment of patients with peripheral artery disease. Participants are instructed to when pain starts in either leg and to continue on the treadmill without stop-ping at this stage. Distance walked is pain-free walking distance. Endpoint was evaluated based on data from in-study observation period. In-study observation period is defined as the period from date of randomisation to one of the following dates, whichever comes first: date of follow-up visit, date when participant withdrew consent, date of last contact with participant for participants who were lost to follow-up (participant did not complete the trial and did not withdraw consent), date of death. Full Analysis Set (FAS). Overall Number of Participants Analyzed = number of participants with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of follow-up (week 57)

End point values	Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	329	333		
Units: Ratio of pain-free walking distance				
median (inter-quartile range (Q1-Q3))	1.18 (0.92 to 1.59)	1.10 (0.83 to 1.48)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in pain-free walking distance on a constant load treadmill test

End point title	Change in pain-free walking distance on a constant load treadmill test

End point description:

The constant-load treadmill test with fixed speed (3.2 km/h, 2 mph), fixed inclination (12%) is a standardised method for functional assessment of patients with peripheral artery disease. Participants are instructed to when pain starts in either leg and to continue on the treadmill without stopping at this stage. Distance walked is pain-free walking distance. Endpoint was evaluated based on data from in-study observation period. In-study observation period is defined as period from date of randomisation to one of following dates, whichever comes first: date of follow-up visit, date when participant withdrew consent, date of last contact with participant for participants who were lost to follow-up (participant did not complete the trial and did not withdraw consent), date of death. Full Analysis Set (FAS). Overall Number of Participants Analyzed = number of participants with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 52)

End point values	Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	338	344		
Units: Ratio of pain-free walking distance				
median (inter-quartile range (Q1-Q3))	1.21 (0.92 to 1.52)	1.10 (0.86 to 1.44)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Semaglutide v Placebo
Number of subjects included in analysis	682
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0046
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	The Hodges-Lehmann Estimate
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.033
upper limit	1.197

Secondary: Change in body weight

End point title	Change in body weight

End point description:

Change in body weight from baseline to week 52 in kilogram (kg) is presented. The endpoint is evaluated based on the on-treatment without rescue treatment observation period. This period includes assessments and events for the time period where participants were exposed to trial product and before rescue treatment (medication or revascularisation procedure). Full Analysis Set (FAS). Overall Number of Participants Analyzed = number of participants with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 52)

End point values	Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	310	318		
Units: Kilogram (kg)				
arithmetic mean (standard deviation)	-5.2 (± 4.8)	-1.2 (± 4.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Glycosylated Haemoglobin (HbA1c)

End point title	Change in Glycosylated Haemoglobin (HbA1c)

End point description:

Change in HbA1c from baseline to week 52 in percentage-point is presented. The endpoint is evaluated based on the on treatment without rescue treatment observation period. This period includes assessments and events for the time period where participants were exposed to trial product and before rescue treatment (medication or revascularisation procedure). Full Analysis Set (FAS). Overall Number of Participants Analyzed = number of participants with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 52)

End point values	Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	304	311		
Units: Percentage-point of HbA1c				
arithmetic mean (standard deviation)	-0.8 (± 1.1)	0.2 (± 1.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Low-density lipoprotein (LDL)-cholesterol

End point title	Change in Low-density lipoprotein (LDL)-cholesterol

End point description:

Change in LDL-cholesterol from baseline to week 52 is presented as ratio to baseline. The endpoint is evaluated based on the on-treatment without rescue treatment observation period. This period includes assessments and events for the time period where participants were exposed to trial product and before

rescue treatment (medication or revascularisation procedure). Full Analysis Set (FAS). Overall Number of Participants Analyzed = number of participants with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 52)

End point values	Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294	296		
Units: Ratio of LDL				
geometric mean (geometric coefficient of variation)	0.99 (± 38.37)	1.03 (± 42.27)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in total cholesterol

End point title	Change in total cholesterol

End point description:

Change in total cholesterol from baseline to week 52 is presented as ratio to baseline. The endpoint is evaluated based on the on-treatment without rescue treatment observation period. This period includes assessments and events for the time period where participants were exposed to trial product and before rescue treatment (medication or revascularisation procedure). Full Analysis Set (FAS). Overall Number of Participants Analyzed = number of participants with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 52)

End point values	Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	305	312		
Units: Ratio of total cholesterol				
geometric mean (geometric coefficient of variation)	0.96 (± 20.18)	1.00 (± 19.88)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in systolic blood pressure

End point title	Change in systolic blood pressure

End point description:

Change in systolic blood pressure from baseline to week 52 is presented. The endpoint measure is evaluated based on the on treatment without rescue treatment observation period. This period includes assessments and events for the time period where participants were exposed to trial product and before rescue treatment (medication or revascularisation procedure). Full Analysis Set (FAS). Overall Number of Participants Analyzed = number of participants with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 52)

End point values	Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	310	319		
Units: Millimetre of mercury (mmHg)				
arithmetic mean (standard deviation)	-4 (± 15)	-1 (± 18)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Ankle–Brachial Index (ABI)

End point title	Change in Ankle–Brachial Index (ABI)

End point description:

Change in ABI from baseline to week 52 is presented. ABI is calculated as a ratio of the higher ankle systolic pressure to the higher systolic pressure measured in both arms. ABI is measured at both left and right leg and the analysis endpoint is defined as the lower of the two indices. An ABI between 1.0 to 1.4 is considered the normal range. An ABI between 0.90 to 0.99 is considered borderline. An ABI less than 0.90 indicates peripheral artery disease (PAD). The endpoint is evaluated based on the on-treatment without rescue treatment observation period. This period includes assessments and events for the time period where participants were exposed to trial product and before rescue treatment (medication or revascularisation procedure). Full Analysis Set (FAS). Overall Number of Participants Analyzed = number of participants with available data for this endpoint.

End point type	Secondary

End point timeframe:

From screening (week -2) to end of treatment (week 52)

End point values	Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	306	315		
Units: Ratio of ABI				
geometric mean (geometric coefficient of variation)	1.06 (± 34.0)	1.02 (± 19.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in High density lipoprotein (HDL)-cholesterol

End point title	Change in High density lipoprotein (HDL)-cholesterol

End point description:

Change in HDL-cholesterol from baseline to week 52 is presented as ratio to baseline. The endpoint is evaluated based on the on-treatment without rescue treatment observation period. This period includes assessments and events for the time period where participants were exposed to trial product and before rescue treatment (medication or revascularisation procedure). Full Analysis Set (FAS). Overall Number of Participants Analyzed = number of participants with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 52)

End point values	Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	294	295		
Units: Ratio of HDL				
geometric mean (geometric coefficient of variation)	1.04 (± 15.95)	0.99 (± 13.91)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in triglycerides

End point title	Change in triglycerides

End point description:

Change in Triglycerides from baseline to week 52 is presented as ratio to baseline. The endpoint is evaluated based on the on-treatment without rescue treatment observation period. This period includes assessments and events for the time period where participants were exposed to trial product and before rescue treatment (medication or revascularisation procedure). Full Analysis Set (FAS). Overall Number of Participants Analyzed = number of participants with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 52)

End point values	Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	305	310		
Units: Ratio of triglycerides				
geometric mean (geometric coefficient of variation)	0.80 (± 45.95)	0.95 (± 41.73)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Short Form 36 (SF-36) physical functioning domain

End point title	Change in Short Form 36 (SF-36) physical functioning domain

End point description:

SF-36 is a 36-item patient-reported survey of patient health that measures participant's overall health-related quality of life (HRQoL). SF-36v2 (acute version) questionnaire measured 8 domains of functional health, well-being, 2 component summary scores (physical and mental component summary). 0-100 scale scores from the SF-36 were converted to norm-based scores (Range: 19.03 to 57.60) to enable a direct interpretation in relation to distribution of scores in the 2009 U.S. general population. Positive change score indicates improvement in participant health status. Endpoint is evaluated based on on-treatment without rescue treatment observation period. This period includes assessments, events for time period where participants were exposed to trial product and before rescue treatment (medication or revascularisation procedure). Full Analysis Set (FAS). Overall Number of Participants Analyzed = number of participants with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 52)

End point values	Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	311	320		
Units: Scores on a scale				
arithmetic mean (standard deviation)	2.98 (± 7.32)	1.52 (± 7.17)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Toe–Brachial Index (TBI)

End point title	Change in Toe–Brachial Index (TBI)

End point description:

Change in TBI from baseline to week 52 is presented. TBI is calculated as a ratio of the toe systolic pressure to the higher systolic pressure measured in both arms. TBI is measured at both left and right leg and the analysis endpoint is defined as the lower of the two indices. A TBI range of above or equal to 0.7 is considered normal, whereas a TBI less than 0.7 is considered abnormal. The endpoint is evaluated based on the on-treatment without rescue treatment observation period. This period includes assessments and events for the time period where participants were exposed to trial product and before rescue treatment (medication or revascularisation procedure). Full Analysis Set (FAS). Overall Number of Participants Analyzed = number of participants with available data for this endpoint.

End point type	Secondary

End point timeframe:

From screening (week -2) to end of treatment (week 52)

End point values	Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	297	301		
Units: Ratio of TBI				
geometric mean (geometric coefficient of variation)	1.07 (± 34.4)	1.04 (± 37.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Walking Impairment Questionnaire (WIQ) global score

End point title	Change in Walking Impairment Questionnaire (WIQ) global score

End point description:

WIQ consists of three domains, speed, distance, stair climbing, consisting of in total 14 questions. Each response is weighted based on difficulty of task. Domain scores are determined by dividing weighted answers by maximum possible weighted score, multiplying by 100. Global score is calculated as mean of three domain scores (ranged from 0% to 100%). Global score of 0% represents inabil-ity to perform any of tasks, 100% represents no difficulty with any of tasks. Higher scores indicate better walking ability, less impairment. Endpoint is evaluated based on on-treatment without rescue treatment observation period. This period includes assessments, events for time period where participants were exposed to trial product and before rescue treatment (medication or revascularisation procedure). Full Analysis Set (FAS). Overall Number of Participants Analyzed = number of participants with available data for this endpoint.

End point type	Secondary

End point timeframe:

From baseline (week 0) to end of treatment (week 52)

End point values	Semaglutide	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	312	321		
Units: %-point scores on a scale				
arithmetic mean (standard deviation)	9.48 (± 18.63)	6.51 (± 20.53)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Until week 57	
Adverse event reporting additional description:	
All presented adverse events are treatment emergent adverse events (TEAEs). A Treatment Emergent Adverse Event (TEAE) is defined as an AE with onset in the on-treatment observation period.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	27

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants received once-weekly (OW) subcutaneous injection (s. c.) of placebo matched for semaglutide for 52 weeks.	
Reporting group title	Semaglutide
Reporting group description:	
Participants received once-weekly (OW) subcutaneous injection (s. c.) of semaglutide for 52 weeks. Participants received a dose of 0.25 milligrams (mg) from week 0 to week 4, then the dose was increased to 0.5 mg from week 4 to week 8. From week 8 to week 52, the dosage was 1.0 mg.	

Serious adverse events	Placebo	Semaglutide	
Total subjects affected by serious adverse events			
subjects affected / exposed	78 / 395 (19.75%)	74 / 396 (18.69%)	
number of deaths (all causes)	9	4	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 395 (0.25%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bladder cancer stage 0, with cancer in situ			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial carcinoma			

subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clear cell renal cell carcinoma			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal cancer metastatic			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma stage II			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal carcinoma			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma stage I			

subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic malignant melanoma			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	1 / 395 (0.25%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pancreatic carcinoma metastatic			
subjects affected / exposed	2 / 395 (0.51%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			

subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Accelerated hypertension			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive urgency			
subjects affected / exposed	0 / 395 (0.00%)	2 / 396 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intermittent claudication			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	2 / 395 (0.51%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			

subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	5 / 395 (1.27%)	4 / 396 (1.01%)	
occurrences causally related to treatment / all	0 / 7	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	3 / 395 (0.76%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	2 / 395 (0.51%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tissue discolouration			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			

Scrotal ulcer			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	0 / 395 (0.00%)	2 / 396 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Epistaxis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory arrest			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 395 (0.00%)	2 / 396 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Investigations			
Neutrophil count decreased			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain contusion			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery restenosis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	2 / 395 (0.51%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture displacement			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 395 (0.00%)	2 / 396 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Limb injury			
subjects affected / exposed	1 / 395 (0.25%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematuria			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	5 / 395 (1.27%)	3 / 396 (0.76%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Angina unstable			
subjects affected / exposed	2 / 395 (0.51%)	3 / 396 (0.76%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	2 / 395 (0.51%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 395 (0.25%)	2 / 396 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			
subjects affected / exposed	1 / 395 (0.25%)	2 / 396 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	0 / 395 (0.00%)	2 / 396 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiogenic shock			

subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 395 (0.00%)	4 / 396 (1.01%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	0 / 395 (0.00%)	3 / 396 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 395 (0.25%)	2 / 396 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			

subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	3 / 395 (0.76%)	3 / 396 (0.76%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic neuropathy			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paresis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
IIIrd nerve paralysis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 395 (0.25%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar stroke			

subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 395 (0.25%)	2 / 396 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 395 (0.00%)	2 / 396 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 395 (0.25%)	2 / 396 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	2 / 395 (0.51%)	2 / 396 (0.51%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic nerve disorder			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Abdominal symptom			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic gastritis			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 395 (0.25%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 395 (0.25%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			

subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic pseudocyst			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis haemorrhagic			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomach mass			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic hepatitis			

subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	2 / 395 (0.51%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	1 / 395 (0.25%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 395 (0.00%)	3 / 396 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Intervertebral disc protrusion			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal stenosis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			

subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	2 / 395 (0.51%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain abscess			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	2 / 395 (0.51%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	2 / 395 (0.51%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			

subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 395 (0.25%)	3 / 396 (0.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	5 / 395 (1.27%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotavirus infection			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	1 / 395 (0.25%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic endocarditis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 395 (0.25%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Wound infection			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Alkalosis			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			

subjects affected / exposed	0 / 395 (0.00%)	1 / 396 (0.25%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obesity			
subjects affected / exposed	1 / 395 (0.25%)	0 / 396 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	Semaglutide	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 395 (6.08%)	47 / 396 (11.87%)	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 395 (0.76%)	22 / 396 (5.56%)	
occurrences (all)	4	26	
Infections and infestations			
COVID-19			
subjects affected / exposed	21 / 395 (5.32%)	30 / 396 (7.58%)	
occurrences (all)	21	32	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 November 2020	Due to the Coronavirus disease (COVID-19) pandemic the exclusion and discontinuation criteria were amended to allow for simultaneous participation in trials with the primary objective of evaluating an approved or non-approved investigational medicinal product for prevention or treatment of COVID-19 disease or COVID-19 postinfectious conditions. Additional blood sampling was included for PK assessment. Plasma semaglutide concentrations was used to describe the exposure-response analysis and other updates.
18 April 2023	To strengthen approach of submitting a single trial to have the lower extremity peripheral artery disease (PAD) information accepted into the label. This was achieved by elevating the supportive endpoint "Follow-up change in maximum walking distance on a constant load treadmill test" to confirmatory secondary endpoint with the purpose of ensuring that the follow-up period results are taken into consideration by regulators. Additionally, this amendment includes the inversion of confirmatory endpoints "Change in pain free walking distance on a constant load treadmill test" and "Change in VascuQoL-6 score", as well as a small change in the wording of the secondary objective related to VascuQoL-6 questionnaire, to clarify the measured concepts and other updates.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported